

claim 1 have special and specific reference to bone. *See, e.g.*, Specification, page 10. In contrast, TGF- β 1 reportedly correlates to numerous non-bone related and non-calcification related disorders. Grainger, page 1. Accordingly, the methods and combinations within the scope of Applicant's claims are joined not only by the fact that they are methods for assessing an individual's predisposition to a selected calcification condition status by genotyping the promoter of at least one gene, but by the further feature that the gene to which the promoter belongs is a gene relating to a protein which has a high level of specificity to bone.

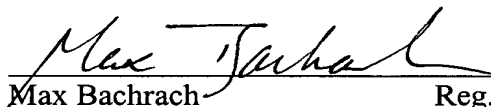
Second, Applicant respectfully submits that an examination of all of the pending claims would not pose a significant burden. This is evidenced by the fact that searches have already been conducted by the European Patent Office in connection with all of the claims. As the Examiner is well aware, "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to distinct or independent inventions." *Manual of Patent Examining Procedure* § 803 (8th ed. August 2001). Therefore, even if the claims did encompass more than one invention, Applicant submits that a requirement that they be examined in separate applications, which would impose upon Applicant significant costs, is inappropriate.²

In sum, Applicant respectfully requests that the restriction requirement be withdrawn. At the very least, however, Applicant respectfully requests that Groups 1, 6 and 7 be examined together.

No fees are believed due for this submission. If any fees are due, however, please charge such fees to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

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² Applicant further submits that an election of species should not be required as to individual polymorphisms within a single specific gene promoter, since a search of all such species would pose little difficulty.